

(FILE 'HOME' ENTERED AT 11:08:56 ON 18 JUL 2002)

FILE 'REGISTRY' ENTERED AT 11:09:04 ON 18 JUL 2002

L1 0 S CDFCFWKTCT/SQEP
L2 0 S CDFCFWKTCT/SQEP
L3 514 S FCFWKTCT/SQEP
L4 0 S L3 AND RADIOMETAL
L5 0 S L3 AND CHELAT?
L6 0 S L3 AND METAL#
L7 0 S L3 AND TUMOR

FILE 'CA' ENTERED AT 11:14:02 ON 18 JUL 2002

L8 1746 S L3
L9 0 S L8 AND RADIO(W)METAL
L10 450 S L8 AND TUMOR
L11 30 S L10 AND CHELAT?
L12 13 S L11 AND IMAG?
L13 17 S L11 NOT L12
L14 0 S L3 AND THIOSEMICARBAZONLYGLYOXYL
L15 0 S L3 AND THIOSEMICARBAZONYLGLYOXYL
L16 (1746) S L3
L17 (1) S THIOSEMICARBAZONYLGLYOXYL
L18 0 S L15 STEP
L19 1 S L17
L20 16507 S SOMATOSTATIN OR OCTREOTIDE
L21 3044 S L20 AND ANALOG?
L22 827 S L21 AND CYCL?
L23 112 S L22 AND TUMOR
L24 1 S L23 AND RADIOIMAGING

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Terms	Documents
L6 and thiosemicarbazonylglyoxyl	0

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L7

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Hit Count Set Name
 result set
DB=JPAB,EPAB; PLUR=YES; OP=OR

<u>L7</u>	L6 and thiosemicarbazonylglyoxyl	0	<u>L7</u>
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<u>L6</u>	somatostatin or octreotide	369	<u>L6</u>
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<u>L5</u>	L4	0	<u>L5</u>
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DB=DWPI; PLUR=YES; OP=OR

<u>L4</u>	L3 and thiosemicarbazonylglyoxyl	0	<u>L4</u>
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<u>L3</u>	somatostatin or octreotide	714	<u>L3</u>
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DB=USPT; PLUR=YES; OP=OR

<u>L2</u>	L1 and thiosemicarbazonylglyoxyl	1	<u>L2</u>
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<u>L1</u>	somatostatin or octreotide	2885	<u>L1</u>
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ILE 'CA' ENTERED AT 13:55:58 ON 18 JUL 2002
L1 0 S PHELYTHIOSEMICARBAZIDYL
L2 0 S PHENYLTHIOSEMICARBAZIDYL
L3 0 S PHENYL(W)THIO(W)SEMICARBAZIDYL
L4 (220411)S PHENYL
L5 (36996)S THIO
L6 (1)S SEMICARBAZIDYL
L7 0 S L3 STEP
L8 1 S L6
L9 132 S THIOCARBZIDE OR THIOCARBAZONE
L10 16 S L9 AND CHELAT?
L11 15 S L10 NOT 1998-2000/PY
L12 117 S L9 NOT L11
L13 0 S L12 AND RADIO(5W) (LABEL OR METAL OR MOIETY)
L14 0 S L12 AND TUMOR
L15 2 S L12 AND IMAG?
L16 2 S THIOSEMICARBAZONYL

L19 ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS

AB The aim of this study was to localize ^{99m}Tc and ^{188}Re radionuclides to tumors, using a bispecific antibody (bsMAb) in a two-step approach where the radionuclides are attached to novel peptides incorporating moieties recognized by one arm of the bsMAb. A chem. cross-linked human/murine bsMAb, hMN-14 .times. 734 (Fab' .times. Fab'), anti-carcinoembryonic antigen [CEA] .times. anti-indium-DTPA was prepd. as a prelude to constructing a fully humanized bsMAb for future clin. application. N,N'-o-Phenylenedimaleimide was used to cross-link the Fab' fragments of the two antibodies at their hinge regions. This construct was shown to

be

>92% pure and fully reactive with CEA and a divalent (indium)DTPA-peptide.

For pretargeting purposes, a peptide, IMP-192

[Ac-Lys(In-DTPA)-Tyr-Lys(In-DTPA)-Lys(TscG-Cys-)-NH₂ {TscG = 3-thiosemicarbazonylglyoxyl}], with two indium-DTPAs and a chelate for selectively binding ^{99m}Tc or ^{188}Re , was synthesized. IMP-192 was formulated in a "single dose" kit

and

later radiolabeled with ^{99m}Tc (94-99%) at up to 1836 Ci/mmol and with ^{188}Re (97%) at 459-945 Ci/mmol of peptide. [^{99m}Tc]IMP-192 was shown to

be

stable by extensive in vitro and in vivo testing and had no specific uptake in the tumor with minimal renal uptake. The biodistribution of

the

hMN-14 .times. murine 734 bsMAb was compared alone and in a pretargeting setting to a fully murine anti-CEA (F6) .times. 734 bsMAb that was reported previously. Both bsMAbs maintained their integrity and dual binding specificity in vivo, but the hMN-14 .times. m734 was cleared more rapidly from the blood. This coincided with an increased uptake of the hMN-14 .times. m734 bsMAb in the liver and spleen, suggesting an active reticuloendothelial cell recognition mechanism of this mixed species construct in naive mice. Animals bearing GW-39 human colonic cancer xenografts were injected with bsMAb (15 .mu.g) and after allowing 24 or

72

h for the bsMAb constructs to clear from the blood (hMN-14 and murine F6 .times. 734, resp.), [^{188}Re]IMP-192 (7 .mu.Ci) or [^{99m}Tc]IMP-192 (10 .mu.Ci) was injected at a bsMAb:peptide ratio of 10:1. Tumor uptake of [^{99m}Tc] or [^{188}Re]IMP-192 was 12.6 .+-. 5.2 and 16.9 .+-. 5.5% ID/g at 3

h

postinjection, resp. Tumor/nontumor ratios were between 5.6 and 23 to 1 for every major organ, indicating that early imaging with ^{99m}Tc will be possible. Radiation absorbed doses showed a 4.8-, 7.2-, and a 12.6 to

1.0

tumor to blood, kidney, and liver ratios when ^{188}Re was used. Although this new bsMAb pretargeting approach requires further optimization, it already shows very promising targeting results for both radioimmunodetection and radioimmunotherapy of colorectal cancer.

=> d l19 ti au so py

L19 ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS

TI Experimental Pretargeting Studies of Cancer with a Humanized anti-CEA .mu.e Murine anti-[In-DTPA] Bispecific Antibody Construct and a ^{99m}Tc -/ ^{188}Re -Labeled Peptide

AU Karacay, H.; McBride, W. J.; Griffiths, G. L.; Sharkey, R. M.; Barbet, J.;

Hansen, H. J.; Goldenberg, D. M.

SO Bioconjugate Chemistry (2000), 11(6), 842-854
CODEN: BCCHES; ISSN: 1043-1802
PY 2000

L24 ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS
AB Title compds. (I; R = H, alkyl, carboxyalkyl; R1 = H, protecting group;
R1R1 = bond between the 2 S atoms; R3 = H, protecting group; A = Q1, Q2,
Q3; m, n = 1-4), were prepd. Thus, tris(2-aminoethyl)amine and
HOCCMe2SSCMe2CHO were refluxed in EtOH to give the **cyclic**
diimine, which was reduced with NaBH4 in refluxing EtOH to give
2-(3,3,13,13-tetramethyl-1,2-dithia-5,8,11-triazacyclotridecan-8-
yl)ethylamine. This was elaborated to 4-isothiocyanato-N-[2-
(3,3,5,11,13,13-hexamethyl-1,2-dithia-5,8,11-triazacyclotridecan-8-
yl)ethyl]benzamide, which was stirred with [**cyclo**
(Trp-Lys(FMOC)-Val-Lys-NMePhe-Tyr)] in DMF/bicarbonate/phosphate buffer
to give I (R = Me; R1R1 = bond; R3 = FMOC; A = Q3; m = 2).

=> d l24 ti au so py

L24 ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS
TI Preparation of technetium- or rhenium-radiolabeled **somatostatin**
analogs as **radioimaging** agents and radiopharmaceuticals.
IN Flanagan, Richard J.; Dufour, Jean-marc; Hogan, Keith T.
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
PY 1996
1996
1996
1997
2002
1998
2002